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EXAMINER	
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ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,369	FOX ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *4-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 9-13* is/are rejected.

7)☒ Claim(s) *2 and 4-9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13 are presented for examination.

Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) from United Kingdom Application No. 0214784.1 filed June 26, 2002 and Applicant's claim for priority under 35 U.S.C. 119(e) from provisional application number 60/396,780 filed July 17, 2002, is acknowledged. Applicant's Preliminary Amendment filed June 25, 2003 has been received and entered into the application. Accordingly, the present specification at page 1, directly following the title, has been amended.

Claim Objection for Improper Multiple Dependency

Claims 4-8 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). **Accordingly, claims 4-8 not been further treated on the merits**.

Claim Objections-Minor Informalities

Claim 2 is objected to for failing to define the abbreviation "IC_{50}" at its first occurrence in the claims. Claim 2 should be rewritten to read the following:

---2. The use according to claim 1, wherein the inhibitor of PDE5 has an IC_{50} value, the concentration of compound required for 50% inhibition of enzyme activity, of less than 100 nM.---

Claim 9 is objected to for failing to conclude with a period. Appropriate correction is required.

Priority Claim on Oath/Declaration

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on United Kingdom Application No. 0214784.1 filed on June 26, 2002. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath/declaration does not acknowledge the filing of any foreign application. Submission of a new oath/declaration with reference to the foreign application is required. See MPEP §202.01 and §202.04 and 37 C.F.R. 1.63 and 1.78.

Missing Residence and Postal Addresses on Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by serial number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because it does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either on an application data sheet or supplemental oath or declaration. Appropriate correction is required.

Title of the Invention

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: --- PHARMACEUTICAL COMPOSITIONS COMPRISING A PDE5 INHIBITOR AND AN

ANGIOTENSIN II RECEPTOR ANTAGONIST FOR THE TREATMENT OF HYPERTENSION---.

Specification Objection

The Examiner has noted the incorporation by reference of International Patent Publications in the present specification at page 6, lines 1-17, for example, of the disclosure. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by a statement executed by the Applicant, or a practitioner representing the Applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. See 37 C.F.R. 1.57(f). Applicant is reminded that the citation of this portion of the disclosure at page 6, lines 1-17, may not reflect all of the places at which the improper incorporation by reference of foreign patent documents occurs. Appropriate correction to all instances of improper incorporation by reference is required.

Claim Rejection-35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 and 9 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a

process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of hypertension using a combination of an inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) and an angiotensin II receptor antagonist, does not reasonably provide enablement for the cure or prevention of the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;
2) the breadth of the claims;

3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;
6) the quantity of experimentation necessary;
7) the state of the prior art; and,
8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

Factors 1 and 2) The claimed invention is directed to the use of a combination of an inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) and an angiotensin II receptor antagonist for the preparation of a medicament for the palliative, curative or prophylactic treatment of hypertension, including essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis and renovascular hypertension, congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance. Particular PDE5 inhibitors and angiotensin II receptor antagonists are recited in the present claims (see present claims 1-3, 9 and 13). Also provided are claims directed to a pharmaceutical composition comprising a cGMP specific PDE5 inhibitor in combination with an angiotensin II receptor antagonist and a kit comprising the same (see present claims 10-12).

Factor 3) There is a known unpredictability in the art when engaging in the prevention of hypertension, since the etiology of the condition is not known but has been suggested to be

related, in part, to heredity, although the mechanism by which that occurs is unclear. The Merck Manual of Diagnosis and Therapy (Sixteenth Edition) notes, "...it seems improbable that a single cause will explain its diverse hemodynamic and pathophysiologic derangements" (Ch.24, p.413, second paragraph from the bottom of the page). Pharmacologic therapies, such as thiazide and related sulfonamide diuretics, loop diuretics, potassium-sparing diuretics, beta blockers, angiotensin converting enzyme inhibitors, calcium antagonists, adrenergic inhibiting agents and behavioral modifications, such as weight loss, restricted alcohol consumption and regular moderate exercise (see The Merck Manual, p.419 "Nonpharmacologic Therapy"), are known in the art to treat the symptoms associated with hypertension. Conventional therapies used for the treatment of hypertension are used to ameliorate and control the symptoms associated with the condition. However, the art does not recognize any type of therapeutic modality to cure or prevent such a condition, primarily because the etiology and risk factors associated with the development of hypertension are elusive and not particularly well characterized (see The Merck Manual, p. 413 and 419-426).

Factor 4) Applicant has merely disclosed that by administering the claimed active composition in a patient with hypertension, one may treat or prevent such a condition in a patient. Based on the discussion in Section 3 above, however, such disclosure clearly is not adequate direction or guidance as to how the proposed active agent(s) could be employed to accomplish the prevention of hypertension in a predictable manner.

Factor 5) The specification at pages 19-20 discloses that use of the presently claimed active composition has activity in the treatment of hypertension in an animal model of human hypertension. Although Applicant discloses that prevention may be achieved, in the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing hypertension or how a patient could be kept from ever developing this condition. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active agent for the prevention of such a condition.

The Examiner acknowledges that the Office does not require the presence of working examples to be present in the disclosure of the invention (see MPEP §2164.02). However, in light of the state of the art, which recognizes particular conventional therapies, such as thiazide and related sulfonamide diuretics, loop diuretics, potassium-sparing diuretics, beta blockers, angiotensin converting enzyme inhibitors, calcium antagonists, adrenergic inhibiting agents and behavioral modifications, (See Factor 7, below), effective in the treatment of hypertension, the Office would require appropriate disclosure to support the contention that the use of the claim specified active composition could actually prevent hypertension or the symptoms associated with such a condition by simply administering, by any method, an amount of the claimed active composition, especially in light of the fact that the present specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing such a condition using the claimed active composition.

Factor 6) The burden of enabling the prevention of hypertension is much greater than that of enabling the treatment of the same condition. Since the present specification would not enable the skilled artisan to prevent hypertension, a clear burden of undue experimentation would be placed upon the skilled artisan in order to practice this aspect of the invention.

Factor 7) Conventional therapies used to treat and control the conditions and symptoms associated with hypertension, such as thiazide and related sulfonamide diuretics, loop diuretics, potassium-sparing diuretics, beta blockers, angiotensin converting enzyme inhibitors, calcium antagonists, adrenergic inhibiting agents and behavioral modifications (see The Merck Manual, p. 413 and 419-426) are well known in the art as treatments for ameliorating the symptoms associated with hypertension. The use of these conventional therapies in patients experiencing hypertension is well known in the art, but is not recognized to have any curative, preventive or prophylactic effect against the development, advancement or cure of such a disease (see Section 3, above). Furthermore, it is more difficult to prevent the development or advancement of hypertension than it is to simply ameliorate the symptoms associated with the condition, especially since it is recognized in the art that there is no known therapeutic modality for the prevention of such a condition.

Factor 8) In view of the discussion of each of the preceding seven factors, the level of skill in this art is high and is at least that of a medical doctor with several years of experience in the art.

Summary

As the cited art and discussion of the above 8 factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that the prevention of hypertension could be achieved. In order to actually achieve prevention of this condition, it is clear from the discussion above that the skilled artisan could not rely on Applicant's disclosure as required by 35 U.S.C. §112, first paragraph. Given that the art fails to recognize and Applicant has failed to demonstrate that hypertension could actually be prevented, the skilled artisan would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention. Accordingly, claims 1-3 and 9 are deemed properly rejected.

Suggestion for Overcoming the Rejection

In order to overcome the present rejection, Applicant may wish to consider amending the claims in the following manner:

---1. The use of a combination of an inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) and an angiotensin II receptor antagonist for the preparation of a medicament for the palliative~~, curative or prophylactic~~ treatment of hypertension, including essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis and renovascular hypertension, congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance.---

Claim Rejection - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 9 provide for the use of a combination of an inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) and an angiotensin II receptor antagonist in the treatment of hypertension, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

For the purposes of examination, claims 1-3 and 9 will be treated as method claims.

Legal Standard for Anticipation/Inherency Under - 35 USC § 102

To anticipate a claim under 35 U.S.C. 102, a single prior art reference must place the invention in the public's possession by disclosing each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to practice the invention. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1001 (Fed. Cir. 1991); *In re Donahue*, 766 F.2d 531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). In order to anticipate, the prior art must either expressly or inherently disclose every limitation of the claimed invention. *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365, 52 U.S.P.Q.2d 1303, 1303 (Fed. Cir. 1999) (citing to *In re Schreiber*, 128 F.3d 1473, 1477, 44 U.S.P.Q.1429, 1431 (Fed. Cir. 1997)); *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 U.S.P.Q.2d 1943, 1946 (Fed. Cir. 1999). In order to inherently anticipate, the prior art must

necessarily function in accordance with, or include, the claimed limitations. *MEHL/Biophile,* 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. However, it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art. *Id.* Specifically, discovery of the mechanism underlying a known process does not make it patentable.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 9-11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Macor et al. (U.S. Patent No. 6,087,368; 2000). Macor et al. teaches the use of a quinazolinone compound and salts thereof as inhibitors of cyclic guanosine monophosphate phosphodiesterase, especially Type V (also known as cGMP PDE Type 5) in the treatment of disorders responding to the inhibition of cGMP PDE, particularly cardiovascular disorders, such as hypertension, angina (including stable, unstable and variant), congestive heart failure, atherosclerosis and stroke (col.1, lines 55-61 and col.16, line 66-col.17, line 9). Macor et al. teaches that the disclosed cGMP PDE Type 5 inhibitor may be employed in combination with other suitable therapeutic agents useful in the treatment of cGMP-associated conditions, such as other cGMP PDE Type 5 inhibitors or angiotensin II antagonists (col.18, line 60-col.19, line 3). Such other agents include sildenafil (col.19, line 6), losartan, irbesartan, valsartan or candesartan (col.19,

lines 10-11), and PDE Type 5 inhibitors, such as the carbazoles taught in WO 95/19978 (col.19, lines 14-15). The disclosure of Macor et al. also teaches the use of other therapeutic agents in combination with the cGMP PDE Type 5 inhibitor, which may be administered prior to, simultaneously with or following the administration of the cGMP inhibitor (col.17, lines 22-25). Furthermore, Macor et al. discloses pharmaceutical compositions comprising a cGMP PDE Type 5 inhibitor, a pharmaceutically acceptable vehicle or diluent and may contain other therapeutic agents (col.17, lines 26-38), such as other cGMP PDE5 inhibitors or angiotensin II antagonist (col.18, lines 60-66). The compositions may be administered in a single dose or as individual divided doses from one to four times per day (col.18, lines 42-48). Macor et al. teach dosage amounts of 0.05 to 100 mg/kg of body weight of active compound per day (col.18, lines 42-48).

Although Macor et al. does not expressly state the condition of hypertension associated with atherosclerosis, the reference discloses the use of a cGMP PDE5 inhibitor in combination with an angiotensin II antagonist for the treatment of hypertension and also for the treatment of atherosclerosis. Thus, the treatment of hypertension associated with the condition of atherosclerosis is within the scope of the invention disclosed by Macor et al. and thus anticipates the limitation of "hypertension associated with atherosclerosis" as recited in present claim 1.

Present claim 13 states, "...an effective amount of an inhibitor of PDE5..." (see present claim 13 at lines 2-3). The Examiner has noted Applicant's disclosure at page 14, lines 23-31, which states the dosage of PDE5 inhibitor "...in the range of from 1 to 500 mg...a preferred dose is in the range 10 to 100 mg of PDE5 inhibitor...". Applicant also discloses at page 14,

lines 18-20 that the "following dosage levels and other dosage levels herein are for the average human subject having a weight range of about 65 to 70 kg". Macor et al. teaches a dose of cGMP PDE Type V inhibitor from about 0.05 to 100 mg/kg of body weight per day (col.18, lines 42-46), which corresponds to 3.25-6500 mg/day for a 65 kg human or 3.5-7000 mg/day for a 70 kg human. The range of 10 to 100 mg underlying the phrase "an effective amount of an inhibitor of PDE5" recited in present claim 13 is clearly within the range taught by Macor et al. and, thus, Macor et al. directly anticipates this limitation of the present claim. See MPEP §2131.01 regarding rejections under 35 U.S.C. 102 of ranges.

Rejection of Claims 2-3 Based on Inherency

It is recognized that the prior art teachings of Macor et al. do not expressly recite a 50% inhibitory concentration (IC_{50}) value of less than 100 nM or less than 50 nM, but the reference does, however, teach a method of treating hypertension, atherosclerosis, congestive heart failure, angina or stroke using a cGMP PDE5 inhibitor in combination with an angiotensin II receptor antagonist (col.1, lines 55-61, col.16, line 66-col.17, line 9, col.18, line 60-col.19, line 3, col. 19, line 6, 10-11 and 14-15, for example). However, because the particular method steps and compounds that are present in the instant claims are also in the patent, it is deemed that the IC_{50} value of the compound of the prior art would have been inherent, whether recognized by the patentees or not. The claiming of a new use, new function or **unknown property** that is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 U.S.P.Q. 430, 433 (CCPA 1977). See also MPEP §2112. It is irrelevant that the prior art observers did not recognize the property or function of the disputed claims; if

the prior art inherently possesses that characteristic, it anticipates. Applicant's attention is further drawn to the MPEP at §2113, which states, "As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). Thus, claims 2-3 are properly rejected as being anticipated by Macor et al.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macor et al. (U.S. Patent No. 6,087,368; 2000), as recited above, in view of The Merck Manual of Diagnosis and Therapy (Sixteenth Edition; 1992, p.413-431), Cecil's Textbook of Medicine (Twenty-First Edition, 2000, 273-279 and 1279-1285), and Physician's Desk Reference, (55th Edition, 2001; p.323 and 330).

The differences between the Macor et al. reference and the presently claimed subject matter lie in that the reference does not teach:

(i) the treatment of essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, renovascular hypertension, diabetes and impaired glucose tolerance;

(ii) a kit comprising a composition of PDE5 inhibitor, a composition of angiotensin II receptor antagonist, and a container for the compositions.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) Macor et al. broadly discloses the use of a cGMP PDE5 inhibitor in combination with an angiotensin II antagonist for the treatment of hypertension, but does not expressly disclose the treatment of the following hypertensive conditions: essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated

with diabetes, renovascular hypertension, diabetes and impaired glucose tolerance. However, such conditions are recognized in the art as hypertensive disorders. The Merck Manual of Diagnosis and Therapy (Sixteenth Edition; 1992) acknowledges the following types of hypertensive disorders as known in the art: primary or essential hypertension (p.413, second paragraph from bottom of page), secondary hypertension (p.415, para.5-6), isolated systolic hypertension (p.419, para.4) and renovascular hypertension (p.415, para.7). Furthermore, Cecil's Textbook of Medicine (Twenty-First Edition, 2000) teaches that pulmonary hypertension was known in the art as a condition resulting in elevated pressure within the pulmonary arterial vessel system (p.273, col.2, para.1-2). Cecil's also teaches the condition of hypertension associated with the disease diabetes, especially in patients with obesity and insulin resistance (p.1284, col.1, para.2-col.2, para.1). It would, therefore, have been obvious to the skilled artisan at the time of the invention to use the pharmaceutical composition comprising a cGMP PDE5 inhibitor in combination with an angiotensin II antagonist as disclosed in Macor et al. not only for the treatment of hypertension, but also for the treatment of other hypertensive conditions, since the composition would be reasonably expected to exert the same or similar function in patients with the above-mentioned hypertensive conditions.

(ii) Although Macor et al. does not expressly disclose a kit formulation of a cGMP PDE5 inhibiting composition and an angiotensin II receptor antagonist composition, it was well known in the art that both cGMP PDE5 inhibiting compositions, such as sildenafil, and angiotensin II receptor antagonist compositions, such as losartan, were available as a discrete pharmaceutical tablet formulations (see Physician's Desk Reference, 55th Edition, 2001; p.323 for VIAGRA® (sildenafil) and 330 for COZAAR® (losartan)). It would, therefore, have been obvious to a

person of ordinary skill in the art at the time of the invention to place each of the discrete tablet formulations into one container for dispensation to a patient receiving a combination therapy of a cGMP PDE5 inhibitor in combination with an angiotensin II antagonist. Such a person would have been motivated to do so in order to facilitate administration and patient compliance with the therapeutic regimen. The Examiner has noted the limitation of "for treating hypertension" in present claim 12, but this is recognized to be a statement of intended use and is not considered to impart any material or physical property to the kit.

Conclusion

Rejection of claims 1-3 and 9-13 is deemed proper.

Claims 4-8 have not been treated on the merits due to improper multiple dependency.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (8:30 AM-6:00 PM), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leslie A. Royds
Patent Examiner
Art Unit 1614

March 2, 2005

RAY HENLEY
PRIMARY EXAMINER
Au1614